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| (21) International Application Number: PCT/US99/26223 (22) International Filing Date: 5 November 1999 (05.11.99) (30) Priority Data: 60/107,710 9 November 1998 (09.11.98) US (63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Application US 60/107,710 (CON) Filed on 9 November 1998 (09.11.98) (71)(72) Applicants and Inventors: NEWMAN, Ira, Jay [US/US]; 2805 East Oakland Park Boulevard, #600, Fort Lauderdale, FL 33306 (US). WASHBURN, David [US/US]; 308-A Pine Street, West Palm Beach, FL 33407 (US). (74) Agent: HEINES, Henry, M.; Townsend and Townsend and Crew LLP, 8th floor, Two Embarcadero Center, San Francisco, CA 94111 (US). | | (81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> |
| (54) Title: IONIC SILVER COMPLEX (57) Abstract The invention relates to a substantially non-colloidal solution made by combining ingredients comprising (a) water; (b) a source of free silver ions; and (c) a substantially non-toxic, substantially thiol-free, substantially water-soluble complexing agent. | | |

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Ionic Silver Complex

CROSS-REFERENCE TO RELATED APPLICATIONS:

This application claims priority to U.S. Provisional Patent Application No. 60/107710, filed November 9, 1998.

5 BACKGROUND OF THE INVENTION:

Field of the Invention:

This invention relates to solutions including complexed ionic silver. More particularly, it relates to solutions including complexed ionic silver wherein the solutions convey health benefits through their use or
10 application.

Description of Related Art:

Silver has been known to act antimicrobially as an agent in and on the body of humans as well as other animals, and to be relatively non-toxic to mammalian cells when used in the minute quantities needed to be
15 antimicrobially effective. The most effective form of silver for antimicrobial use is as ions in solution. Silver ions have been shown in the past to have antibacterial, antiviral and antifungal qualities, and to contribute directly to the regeneration of tissue. While the exact method by which silver ions perform these functions is not known, it is believed that they may (1)
20 disrupt the respiratory functions, or (2) disrupt membrane functionality of single-celled microorganisms, or (3) link to the cell's DNA and disrupt cell functions. It is not conventionally understood why silver ions appear to some to be effective at regenerating tissue, which apparently involves more than acting as an antimicrobial agent.

25 During recent years, ionic silver substances have been undergoing a substantial resurgence in popularity, and are increasingly regarded as a reasonably safe and effective antimicrobial agent. Silver ion substances are increasingly being used in medical applications as well as by those

seeking a natural alternative to traditional antibiotic medications. Ionic silver substances are being used in topical dressings to treat wounds and to prevent and treat infections. They are also being used for water supply sanitation for public utilities, for pharmaceutical equipment sanitation, and
5 for killing germs including the germ that causes Legionnaires' Disease in the water systems of hospitals. Tooth brushes are now being introduced that release silver ions in order to fight oral bacteria.

However, delivering silver ions for utilization in or on the body is a challenge because silver ions are electrically attracted to a host of
10 substances in and on the body, resulting in the silver ions rapidly forming complexes or compounds wherein the ion is no longer available to perform the appropriate antimicrobial function. A controlled, gradual release of silver ions is desirable for achieving appropriate use of silver ions in or on the body in order to offset this phenomenon, and is
15 especially challenging for antimicrobial use of silver ions internally such as upon oral ingestion. If free silver, defined as silver ions which are not part of a complex or compound, and are therefore biologically available, are delivered at once to the body, there is only opportunity for them to perform the antimicrobial function for an instant where they make contact with the
20 body or the oral tissue before being rendered inactive.

The desirable characteristics of an antimicrobial ionic silver formulation are that it gradually releases its silver content as free silver ions upon ingestion or upon topical application in a manner that is slow enough to sustain the antimicrobial functionality for a sufficient period of
25 time while also being rapid enough to be substantially effective, that it facilitate mobility of the silver through the body upon oral ingestion prior to gradually releasing its silver content as available free silver ions, and that it be nontoxic to the body.

Topical applications of ionic silver do not require a controlled,
30 gradual release of silver ions to the degree that internal, oral ingestion applications require it because there is a lower presence of agents with

which the silver ions can bind up and form complexes or compounds upon topical exposure as compared with ingestion for internal use. At least one product has been recently introduced that consists of a film dressing impregnated with a complex that gradually releases silver ions upon exposure to the body's chemistry.

Previously, some silver-containing chemical substances, such as silver nitrate, have been utilized in an effort to gain the antimicrobial benefits of silver ions, but these substances have proven minimally effective in or on the body because they immediately deliver all of their silver content as free silver ions. Some such substances, such as silver nitrate, are undesirably toxic to the human body when administered in typical doses.

Colloidal silver is a substance which has been in use for about a hundred years. It provides a reasonable degree of controlled release and mobility of silver ions in and on the body. Colloidal silver is apparently made up of minute particles of silver, associated with silver ions that comprise a small percentage of such particles. The mass of these particles provide a degree of controlled, gradual release of silver ions as the body's chemistry breaks down these particles.

However, the electrolysis process that is used to make most colloidal silver has substantial limitations and does not enable adequate consistency in terms of parts per million (PPM) of silver relative to the total solution by molar weight, particle size, or percentage of ions, for most desired applications. Additionally, purity of the substance is typically limited because electrolytes must usually be added to the water during the production method, the most common of which is sodium. Oxides typically form during production, often resulting in an undesirable yellow or brown color. Moreover, the potency of most electrically produced colloidal silver is inherently limited. After a concentration of approximately 5 PPM of silver (in some cases up to approximately 20 PPM of silver) is reached, the production method typically fails to continue yielding electron-deficient

silver particles. The particles formed after such a concentration is reached are typically not capable of performing antimicrobial functions as do the particles that are initially produced prior to reaching this approximate level of total silver concentration (the aggregate of the complexed silver and the
5 free, available silver in the water-based solution).

The term colloidal means "something suspended in a dissimilar medium," and shelf life is, therefore, inherently limited because the colloidal silver particles gradually settle out of the water. Colloidal particles are not dissolved in the water medium; they are not in solution. The
10 suspension is a result of, for example, Brownian motion which is insufficient to keep the particles from settling out over time. Some colloidal silver substances have stabilizing agents such as proteins added to the formula, but these tend to further hinder the availability of the silver ions to the body. What is therefore needed are compositions comprising
15 silver ions, and methods of making and using such compositions, that address the aforementioned problems.

SUMMARY OF THE INVENTION:

In an aspect, the invention relates to a substantially non-colloidal solution made by combining ingredients comprising (a) water; (b) a source
20 of free silver ions; and (c) a substantially non-toxic, substantially thiol-free, substantially water-soluble complexing agent.

DETAILED DESCRIPTION:

The inventors have unexpectedly discovered that a substantially non-colloidal solution made by combining ingredients comprising (a)
25 water; (b) a source of free silver ions; and (c) a substantially non-toxic, substantially thiol-free, substantially water-soluble complexing agent overcomes many of the limitations inherent in the aforementioned forms of ionic silver substances and has wide application in and on the body.

The inventive, substantially non-colloidal solution provides silver ion concentrations well above those typically provided by colloidal silver products. The production method provides a typically consistent formulation. The inventive formulation is highly stable, has many years of shelf life, and maintains its consistency and structure under a wide range of environmental conditions. Substantially wide concentration ranges of complexed silver are attainable without significantly compromising the desirable characteristics of the product. The composition of the invention efficiently provides for substantial mobility of the silver complex through the body and for controlled decomplexing of its silver content, whereupon it gradually releases silver as available free silver ions, upon introduction of the product to the body's chemistry internally through oral ingestion or upon topical application.

Further, the inventive, substantially non-colloidal solution is relatively nontoxic to the human body at typical doses.

The inventive substantially non-colloidal solutions are made from ingredients comprising water, a source of free silver ions; and a substantially non-toxic, substantially thiol-free, substantially water-soluble complexing agent.

Water usable in the practice of this invention should be relatively pure. Suitable types of water include: deionized water, distilled water, reverse osmosis filtered water, reagent grade water and USP grade water suitable for use in pharmaceuticals. The water is desirably substantially free of contaminants, such as parasites, pathogens, chemical contaminants, and particulate contamination.

The source of silver ions may be virtually any compound or complex which includes silver ions as a constituent, from which those silver ions can be obtained in order to be complexed with the recited complexing agent or to become free silver ions as part of the inventive solution. Sources of silver ions comprise silver oxide, trisilver citrate, silver acetate, water soluble silver salts or any number of other sources of

silver without departing from the scope of the invention. In a preferable embodiment, the source of silver ions is silver oxide (AgO). On complexing, silver oxide eliminates a superfluous counter ion, hydroxide, which is innocuous since hydroxide is already present in the solution.

5 The substantially non-toxic, substantially thiol-free, substantially water-soluble complexing agent serves primarily to provide a "controlled release" of biologically active silver ions. In the context of the invention, complexing agent may be taken to mean an ionic material with which silver ions are complexed in such a manner that the complexing agent
10 forms a weak bond with the silver ions wherein the missing electron position which is a characteristic of the silver ion is filled by an electron of the complexing agent. The substantially non-toxic, substantially thiol-free, substantially water-soluble complexing agent may comprise a carboxylic acid, or a primary, secondary or tertiary amine. In the context of this
15 invention, substantially non-toxic may be taken to mean that the recited complexing agent, when present in the inventive solution in usual amounts according to the invention, and when administered as part of the inventive solution in usual dosage amounts of the inventive solution, creates little or no toxic effects in a host to which the inventive solution is
20 administered. In an embodiment, the substantially non-toxic, substantially thiol-free, substantially water-soluble complexing agent comprises amino acids or hydroxy acids. In a preferable embodiment, the amino acids comprise glycine, alanine, valine, leucine, isoleucine, methionine, proline, phenylalanine, tryptophan, serine, threonine, tyrosine,
25 asparagine, glutamine, aspartic acid, glutamic acid, lysine, arginine, or histidine. In another preferable embodiment, the hydroxy acids comprise glycolic acid, lactic acid, malic acid, tartaric acid, citric acid, or mandelic acid. In a more preferable embodiment, the citric acid comprises dibasic citrate. Citrate, a key constituent of the metabolic system, is
30 aggressively drawn to the cells throughout the body and provides an efficient delivery system for spreading the silver through the body before decomplexing takes place and the silver is gradually released as available

free silver ions. Also useful are acetic acid; certain crown ethers; primary, secondary or tertiary amines, such as ethanolamine, and other conventionally known substantially non-toxic, substantially thiol-free, substantially water-soluble complexing agents.

5 In an embodiment, the inventive substantially non-colloidal solution possesses greater than about twenty parts of silver per million parts of the non-colloidal solution. In the context of this invention, PPM is defined as parts of total silver to 1,000,000 parts of the total solution including the water base and all substances contained in it by weight. In another
10 embodiment, the substantially non-colloidal solution possesses greater than about fifty parts of total silver per million parts of the non-colloidal solution. In a more preferable embodiment, the substantially non-colloidal solution possesses greater than or equal to about one hundred parts of total silver per million parts of the non-colloidal solution. Higher parts per
15 million of total silver are desirable, as biological effectiveness increases as PPM free silver increases.

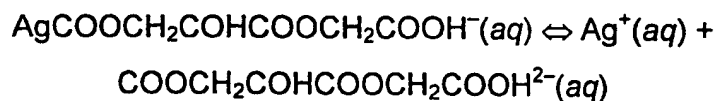
 100 PPM of silver is a desirable level for the total concentration of silver because it provides a highly effective concentration of silver yet the concentration is low enough to facilitate ease of measuring and
20 dispensing the small dosages appropriate for small children and small animals. However, the amount of silver can vary substantially, within solubility limits, without departing from the scope of the invention, as long as the other elements are varied in relative proportion to the silver. In another embodiment, the inventive solution may be comprised of as little
25 as about 10 PPM of silver or as much as about 10,000 PPM of silver without departing from the scope of the invention.

 In an aspect of the invention, counter ions may be utilized. Such counter ions may be used to balance the charge present in the recited complexing agent, if necessary. Sources for counter ions suitable for use
30 in this invention include those conventionally known sources of counter ions. Any suitable source of counter ions may be used where the

complexing agent is such that a counter ion is required to maintain the electrical stability of the silver complex, so long as the counter ion used does not compete with the silver for the complexing agent. In a preferable embodiment, the source of counter-ions comprises potassium ions, or
5 calcium ions.

In an aspect of the invention, the inventive non-colloidal solution possesses less than about ten weight percent of free silver based on the weight of total silver. In an aspect of the invention, the non-colloidal solution possesses less than about one weight percent of free silver
10 based on the weight of total silver. In an aspect of the invention, the non-colloidal solution possesses less than about one-tenth of a weight percent of free silver based on the weight of total silver. A relatively low amount of free silver as compared to total silver (including non-free silver or complexed silver), is retained in a non-reacted state in the inventive
15 solution, until released over time by the equilibrium driving force. This controlled release aspect of the inventive formulation is desirable, as activity is retained over time.

The preferred embodiment of the invention, containing a complex of citrate and silver with potassium as a counter ion, may include the
20 following complex of ions in a solution of relatively pure water:



In a preferable embodiment the inventive solution may be made by mixing silver oxide, citric acid and tripotassium citrate in an approximately
25 1:4:4 molar ratio, respectively, in sufficient pure water to produce a silver concentration of 100 parts per million. Other formulations which result in an approximate 1:2 molar ratio to an approximate 1:20 molar ratio of silver to dibasic citrate in no way depart from the scope of the invention. Generally, a preferable molar ratio (as dry ingredient or as solution) of
30 silver to complexing agent is from about 1:1 to about 1:200, more

preferably from about 1:1.5 to 1:50, most preferably from about 1:2 to about 1:20.

In another preferable embodiment, the free silver ions are present in the substantially non-colloidal solution in an anti-microbially effective
5 amount.

The inventors have also produced the product following the general procedures described above but reducing the amounts of citric acid and of potassium citrate to half of the amounts described above. Numerous other variations can also be utilized with these starting ingredients provided that
10 the ratio of citric acid to potassium citrate is generally maintained. Likewise, the amount of silver oxide may be substantially increased or decreased provided that a reasonably commensurate adjustment is made in the relative amounts of citric acid and of potassium citrate to silver oxide although, as demonstrated by the fact that the product was
15 successfully produced upon changing the ratio of silver oxide to citric acid and to potassium citrate by 100%, substantial latitude exists with regard to that ratio.

As previously stated herein, numerous alternative source ingredients for yielding the silver ion, complexing agent, and counter ion
20 for the preferred embodiment of the invention may also be used, requiring appropriately adjusted quantities, and, likewise, numerous other complexing agents and, if required, counter ion agents, may be selected as the constituents of the product as well, also requiring the appropriately adjusted quantities of the appropriate source ingredients necessary to
25 produce the desired product.

It has often been claimed that ionic silver can kill over 650 disease-causing germs. The invention is absolutely harmless to the body when used in the low quantities needed for the antimicrobial action to occur, especially since the formulation provides an efficiently controlled, gradual
30 release of free silver ions (provided that the complexing agent is nontoxic), requiring less silver ingestion in order to obtain the benefits of

silver ion activity that other substances cannot render with substantially higher levels of silver ingestion.

5 Ionic silver is used for literally hundreds of conditions, including eye and ear infections, nose, sinus and gum infections, acne, sore throats, colds and flu, candida, bladder and vaginal infections, cuts and burns, many skin conditions, bug bites, fighting nail and skin fungus, healing sunburn, alleviating diaper rash and bed sores, providing a soothing skin treatment after shaving, and use as a mouth rinse. Body odors are caused by bacteria in the perspiration, which is often alleviated upon application of the invention, clearly demonstrating how effectively it kills bacteria. Ionic silver is also used for treating ulcers, both in fighting the bacteria that can aggravate an ulcer and in repairing the damaged stomach lining. Ionic silver is used for many severe conditions as well, including, for example, tuberculosis, Epstein-Barr Virus, Lyme Disease, Legionnaires' Disease, bronchitis, chicken pox, and numerous others. There are actually few germ-related conditions, or conditions requiring the repair of tissue, for which ionic silver is not used, since many claim it is not only effective in killing most bacteria but also many if not most fungus and viruses. Some reports indicate that it is also effective against a number of parasites that might invade the body. Ionic silver is also reported by some researchers to be effective at treating cancer and HIV.

25 Other uses for ionic silver range from purifying bottled water by placing some in the water, to retardation of food spoilage at home. Recent studies show that over 30 percent of bottled water contains bacteria levels above safety limits, which can readily be addressed with a few drops of the invention being added to the water. Spraying sliced fruits with the formulation of the invention can keep them fresh up to a week before spoilage, clearly demonstrating how effectively the invention kills bacteria on foods. It is also used to reverse existing contamination of foods.

Ionic silver is also considered by many to be very useful in oral irrigation systems designed for consumer use, that spray a fine stream of water in the mouth, in fighting infection and healing gums. Ionic silver is even reputed t

5 In virtually all applications for which ionic silver is used, the advantages of a relatively high PPM of silver, a controlled, gradual release of available free silver ions and, in the case of the preferred embodiment of the invention, the benefit of citrate as a carrier on internal use together with the lack of toxicity and minimum likelihood of incurring mutated strains of germs, all serve to provide substantially superior
10 benefits to those who would use the product for any of the myriad of conditions for which ionic silver would be used.

The product can readily be bottled or packaged with a variety of types of dispensers to further facilitate its usefulness. A bottle with a dropper is most convenient for eye drops, ear drops and nose drops.
15 Alternatively, a plastic squeeze bottle can serve as a convenient dispenser for eye drops and ear drops, while the same with a nasal sprayer feature can readily facilitate use as a sinus and nasal spray. A spray dispenser such as with, for instance, a pump spray, makes it very convenient to apply the product externally and also provides a convenient
20 and efficient method for oral use and internal ingestion. By disbursing the product upon spraying it in the mouth, such a spray facilitates absorption of the formula into the blood system through the tissue lining in the mouth. A spray dispenser also facilitates delivery of the product to the lungs as one may inhale while spraying the product towards the throat area. while
25 inhaling. Because of the existence of a weak complex of silver and the existence of available free silver ions, along with the photo-reactive qualities of silver, packaging should preferably be in an opaque glass container, in a stainless steel container, or in a polypropylene or polyethylene plastic container. Ideally, dispensers should be made of
30 such materials as well.

Topically applying a gauze, cotton, sheer strip or other type of bandage or fabric that has been saturated with the product is another alternative for using the product.

5 The product can be used for humans as well as animals. When the complexing agent is a nontoxic material, the product is safe for children and pets. Thus, the invention has a wide range of potential uses for both medical and veterinary applications.

10 The product can also be applied to surfaces for killing germs thereon. For instance, it can be sprayed on counter tops, cutting boards, toilet seats, door knobs, telephone handsets, etc. Upon contact with germ cells, the available free silver ions should react with and kill the germ cell, causing another silver ion to be decomplexed and released from the complexing agent and be made available.

15 The invention may be utilized in both the prevention and the treatment of disease.

20 Due to the efficient delivery of silver ions afforded by the invention, an individual may ingest the product on a daily basis as a preventative, achieving substantial levels of protection from germs, while remaining within extremely safe limits of daily and lifelong silver intake relative to the amount of silver contained in the product in the preferred embodiment. Studies show that the amount of silver in the average daily diet of adult Americans was depleted by as much as 85% between the early half of the 20th century and the latter part of that century. With the preferred embodiment of the invention, an individual consuming a substantial
25 amount of the product on a daily basis in terms of potential health benefits would, in fact, be consuming no more silver than that amount which was depleted from the diets over that period of time.

EXAMPLES:**EXAMPLE 1**

5 Two and one-half liters of pure water were placed in a 5-gallon (19-liter functional capacity) carboy mounted on a magnetic stirrer with a Teflon-coated magnetic stir bar placed inside the carboy, turning on the stirrer at low speed, adding 6.7675 grams of citric acid anhydrous powder (reagent grade), 11.43 grams of potassium citrate monohydrate crystal
10 (reagent grade), and 2.2450 grams of silver oxide powder (reagent grade), stirring at low speed for approximately 45 minutes. Next more water was slowly fed while continuing to stir at low speed for approximately an additional 15 minutes and stopping the water input when the level reaches approximately 8-9 liters. Then, the stir speed was
15 turned to high and stirring continued for approximately an additional 30 minutes, filling the carboy to approximately the 18-liter mark, turning off the stirrer, opening the water input valve and stopping the water input at precisely the 19-liter mark, turning the stirrer back on to the high speed, and stirring for an additional 60 minutes.

20 EXAMPLE 2

A 65-year old male developed conjunctivitis and obtained relief within less than five hours upon administering two drops of the solution of Example 1 in his eye.

EXAMPLE 3

25 A sixteen-year-old female had been suffering with acne for three or four years. A dermatologist had been treating her regularly to no avail. She applied six sprays of the solution of Example 1 three times per day to her face for three days and stopped using products from the

dermatologist, and by the end of the third day the skin on her face cleared up almost completely. There was no dryness or redness any more.

EXAMPLE 4

5 A 45-year-old male had been diagnosed with lymphatic cancer and after taking an oral dose of one teaspoon of the solution of Example 1 per day for two months, tests showed that not a trace of the disease remained.

EXAMPLE 5

10 A 31-year-old male and a 28-year-old male who work together in the same store had both come down with a full-blown flu. Both took fifteen drops of the solution of Example 1 in an oral dose, one time, and within a day-and-a-half both were completely free of any further symptoms.

EXAMPLE 6

15 A one-year old male was diagnosed with a blocked tear duct in his left eye. Every day, he awoke with a green drainage that continued through the day. Two physicians recommended surgery. The boys mother administered only one drop of the solution of Example 1 in his eye each day for two days. The condition disappeared. Upon a follow-up nine months later, the condition had not returned.

20 EXAMPLE 7

A 53-year-old woman burned the back of her hand on a 450-degree oven. The burn was approximately an inch-and-a-quarter in diameter. After a week, it still had not begun to heal. The pain was still so bad that she could barely move her hand. She put two drops of the
25 solution of Example 1 on it. By that same night, it had completely scabbed over and the entire circumference of the burn had already generated new tissue. The pain was completely gone and she had regained complete

movement of her hand. Within about four more days of applying the invention, it was completely healed, without any scarring.

EXAMPLE 8

5 A 61-year-old male had developed a urinary tract infection. A urologist put him on sulfa-drugs for twenty days. He suffered through a week of constant nausea, at which point he threw out the remaining pills. He then began to ingest 30 drops of the solution of Example 1 per day, and after three days the infection was no longer detectable.

EXAMPLE 9

10 A forty-four-year-old male developed abscesses surrounding two wisdom teeth. Three oral surgeons told him the teeth had to come out. He applied approximately one teaspoon of the solution of Example 1 each to each of the two affected areas. By the next day, the infections were undetectable and the pain was gone. A follow-up eleven months later
15 showed that it had not returned.

EXAMPLE 10

A twenty-four-year-old woman developed a vaginal infection. The doctor's prescription didn't help after almost two weeks. She then mixed one half-teaspoon of the solution of Example 1 in pure water and used the
20 mixture as a douche, and the discomfort disappeared almost immediately and had not returned upon a follow-up three weeks later.

Claims:

1. A substantially non-colloidal solution made by combining ingredients comprising:
 - (a) water;
 - 5 (b) a source of free silver ions; and
 - (c) a substantially non-toxic, substantially thiol-free, substantially water-soluble complexing agent.
- 10 2. The substantially non-colloidal solution of claim 1, wherein the non-colloidal solution possesses less than about ten weight percent of free silver based on the weight of total silver.
3. The substantially non-colloidal solution of claim 2, wherein the non-colloidal solution possesses less than about one weight percent of free silver based the weight of total silver.
- 15 4. The substantially non-colloidal solution of claim 3, wherein the non-colloidal solution possesses less than about one-tenth of a percent by weight of free silver based on the weight of total silver.
5. The substantially non-colloidal solution of claim 1, wherein the non-colloidal solution possesses greater than about twenty parts of total silver per million parts of the non-colloidal solution.
- 20 6. The substantially non-colloidal solution of claim 5, wherein the non-colloidal solution possesses greater than about fifty parts of total silver per million parts of the non-colloidal solution.
- 25 7. The substantially non-colloidal solution of claim 6, wherein the non-colloidal solution possesses greater than or equal to about one hundred parts of total silver per million parts of the non-colloidal solution.

8. The substantially non-colloidal solution of claim 1, wherein the source of free silver ions comprises silver oxide, trisilver citrate, or silver acetate.
9. The substantially non-colloidal solution of claim 8, wherein the
5 source of free silver ions comprises silver oxide.
10. The substantially non-colloidal solution of claim 1, wherein the substantially non-toxic, substantially thiol-free, substantially water-soluble complexing agent comprises a carboxylic acid, or a primary, secondary or tertiary amine.
- 10 11. The substantially non-colloidal solution of claim 10, wherein the substantially non-toxic, substantially thiol-free, substantially water-soluble complexing agent comprises amino acids or hydroxy acids.
12. The substantially non-colloidal solution of claim 11, wherein the amino acids comprise glycine, alanine, valine, leucine, isoleucine,
15 methionine, proline, phenylalanine, tryptophan, serine, threonine, tyrosine, asparagine, glutamine, aspartic acid, glutamic acid, lysine, arginine, or histidine.
13. The substantially non-colloidal solution of claim 12, wherein the hydroxy acids comprise glycolic acid, lactic acid, malic acid, tartaric acid,
20 citric acid, or mandelic acid.
14. The substantially non-colloidal solution of claim 13, wherein the citric acid is dibasic citrate.
15. The substantially non-colloidal solution of claim 1, wherein the free silver ions are present in the substantially non-colloidal solution in an anti-
25 microbially effective amount.
16. The substantially non-colloidal solution of claim 1, wherein the ingredients further comprise a source of counter-ions.

17. The substantially non-colloidal solution of claim 1, wherein the source of counter-ions comprises potassium ions, or calcium ions.

INTERNATIONAL SEARCH REPORT

Application No

PCT/US 99/26223

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/28 A61K47/12 A61K47/18 A01N37/36

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K A01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
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☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

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Date of the actual completion of the international search

17 February 2000

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Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3018

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